

ARCD:177  
SN 08/455,683

**Appendix A:**

**Marked-up Copy of Claim Amendments**  
**after Second Submission under 37 C.F.R. 1.129**

64. [Cancelled]

91. (Twice amended) A process of screening a substance for its ability to specifically bind to [interact with] an opioid receptor, said process comprising the steps of:

- a) expressing a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:1;
- b) contacting said substance with the opioid receptor polypeptide; and
- c) detecting the ability of said substance to specifically bind to [interact with] said opioid receptor polypeptide.

97. (Twice amended) A process of screening a substance for its ability to specifically bind to [interact with] an opioid receptor, said process comprising the steps of:

- a) expressing a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11;
- b) contacting said substance with the opioid receptor polypeptide; and
- c) detecting the ability of said substance to specifically bind to [interact with] said opioid receptor polypeptide.

103. (Twice amended) A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

- a) providing an opioid receptor polypeptide comprising [a second extracellular loop] SEQ ID NO:17, wherein the polypeptide is [and] encoded for by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:1;

ARCD:177  
SN 08/455,683

- b) contacting said opioid receptor polypeptide with a composition comprising said substance;
- c) detecting the ability of said substance to [interact] act as [an] a specific agonist [with] of said opioid receptor; and
- d) isolating said substance if the ability of said substance to [specifically interact with] act as a specific agonist of the opioid receptor is detected.

109. (Twice amended) A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

- a) providing an opioid receptor polypeptide comprising SEQ ID NO:17 and encoded for by a nucleic acid sequence comprising at least 60 [30] contiguous bases of SEQ ID NO:11;
- b) contacting said opioid receptor polypeptide with a composition comprising said substance;
- c) detecting the ability of said substance to bind to [interact as an agonist with] said opioid receptor polypeptide; and
- d) isolating said substance if the ability of said substance to specifically bind to the opioid receptor polypeptide is detected.

110. [Cancelled]

111. [Cancelled]

112. (Twice amended) The process of claim 109 [111], wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:11.

ARCD:177  
SN 08/455,683

115. [Cancelled]

116. (Amended) The process according to claim [115] 91, wherein said opioid receptor polypeptide is a chimeric opioid receptor polypeptide.

117. (Amended) The process of claim 116, wherein [one polypeptide of] the chimeric opioid receptor polypeptide comprises SEQ ID NO:17 [the second extracellular loop of kappa opioid receptor].

118. (Amended) The process of claim 116, wherein [one polypeptide of] the chimeric opioid receptor polypeptide comprises SEQ ID NO:14 [the third extracellular loop of kappa opioid receptor].

121. (Amended) The process according to claim 91 [115], wherein the opioid receptor polypeptide is a kappa opioid receptor polypeptide having the sequence of SEQ ID NO:2 [or SEQ ID NO:12].

123. (Amended) The process of claim 143 [121], wherein said opioid receptor polypeptide is a kappa opioid receptor polypeptide encoded for by the polynucleotide of SEQ ID NO: 11.

124. [Cancelled]

125. (Amended) The process of claim 103 [124], wherein the opioid receptor polypeptide is a chimeric opioid receptor polypeptide.

126. (Amended) The process of claim 125 [124], wherein one polypeptide of the chimeric opioid receptor polypeptide comprises the third extracellular loop of delta opioid receptor.

ARCD:177  
SN 08/455,683

127. (Amended) The process of claim 125 [124], wherein the opioid receptor polypeptide comprises portions of both kappa and delta opioid receptors.

128. (Amended) The process of claim 125 [124], wherein the chimeric polypeptide comprises  $\kappa_{1-78}/\delta_{70-372}$  or  $\delta_{1-69}/\kappa_{79-380}$ .

129. (Twice Amended) A process of screening a substance for its ability to act as [an] a specific agonist of a kappa opioid receptor comprising:

- a) expressing [either (1)] a chimeric recombinant opioid receptor polypeptide comprising a SEQ ID NO:17, wherein said opioid receptor polypeptide is encoded [for] by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:1 [ or (2) a chimeric recombinant opioid receptor polypeptide comprising the second extracellular loop and encoded for by a nucleic acid sequence comprising a segment consisting of 60 contiguous bases of SEQ ID NO:11];
- b) contacting said substance with the opioid receptor polypeptide; and
- c) detecting the ability of the substance to [interact as an agonist with] specifically bind to the opioid receptor polypeptide.

133. [Cancelled]

136. [Cancelled]

ARCD:177  
SN 08/455,683

**APPENDIX B**  
**PENDING CLAIMS AS OF APRIL 30, 2001**

91. A process of screening a substance for its ability to specifically bind to an opioid receptor, said process comprising the steps of:
- a) expressing a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:1;
  - b) contacting said substance with the opioid receptor polypeptide; and
  - c) detecting the ability of said substance to specifically bind to said opioid receptor polypeptide.
92. The process of claim 91, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 40 contiguous bases of SEQ ID NO:1.
93. The process of claim 92, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 50 contiguous bases of SEQ ID NO:1.
94. The process of claim 93, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:1.
95. The process of claim 94, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 100 contiguous bases of SEQ ID NO:1.
96. The process of claim 95, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 680 contiguous bases of SEQ ID NO:1.
97. A process of screening a substance for its ability to specifically bind to an opioid receptor, said process comprising the steps of:

ARCD:177  
SN 08/455,683

- a) expressing a recombinant opioid receptor polypeptide encoded for by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11;
- b) contacting said substance with the opioid receptor polypeptide; and
- c) detecting the ability of said substance to specifically bind to said opioid receptor polypeptide.

98. The process of claim 97, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 40 contiguous bases of SEQ ID NO:11.

99. The process of claim 98, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 50 contiguous bases of SEQ ID NO:11.

100. The process of claim 99, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:11.

101. The process of claim 100, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 100 contiguous bases of SEQ ID NO:11.

102. The process of claim 101, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 680 contiguous bases of SEQ ID NO:11.

103. (Twice amended) A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

- a) providing an opioid receptor polypeptide comprising SEQ ID NO:17, wherein the polypeptide is encoded for by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:1;

ARCD:177  
SN 08/455,683

- b) contacting said opioid receptor polypeptide with a composition comprising said substance;
- c) detecting the ability of said substance to act as a specific agonist of said opioid receptor; and
- d) isolating said substance if the ability of said substance to act as a specific agonist of the opioid receptor is detected.

104. The process of claim 103, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 40 contiguous bases of SEQ ID NO:1.

105. The process of claim 104, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 50 contiguous bases of SEQ ID NO:1.

106. The process of claim 105, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:1.

107. The process of claim 106, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 100 contiguous bases of SEQ ID NO:1.

108. The process of claim 107, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 680 contiguous bases of SEQ ID NO:1.

109. A process of isolating a substance with an ability to act as a specific agonist of a kappa opioid receptor, said process comprising the steps of:

- a) providing an opioid receptor polypeptide comprising SEQ ID NO:17 and encoded for by a nucleic acid sequence comprising at least 60 contiguous bases of SEQ ID NO:11;

ARCD:177  
SN 08/455,683

- b) contacting said opioid receptor polypeptide with a composition comprising said substance;
- c) detecting the ability of said substance to bind to said opioid receptor polypeptide; and
- d) isolating said substance if the ability of said substance to specifically bind to the opioid receptor polypeptide is detected.

112. (Twice amended) The process of claim 109, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 75 contiguous bases of SEQ ID NO:11.

113. The process of claim 112, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 100 contiguous bases of SEQ ID NO:11.

114. The process of claim 113, wherein said opioid receptor polypeptide is encoded for by a nucleic acid sequence comprising at least 680 contiguous bases of SEQ ID NO:11.

116. The process according to claim 91, wherein said opioid receptor polypeptide is a chimeric opioid receptor polypeptide.

117. The process of claim 116, wherein the chimeric opioid receptor polypeptide comprises SEQ ID NO:17.

118. The process of claim 116, wherein the chimeric opioid receptor polypeptide comprises SEQ ID NO:14.

119. The process of claim 116, wherein the chimeric opioid receptor polypeptide comprises polypeptide portions of both kappa and delta opioid receptors.



ARCD:177  
SN 08/455,683

120. The process according to claim 116, wherein the chimeric opioid receptor polypeptide comprises  $\kappa_{1-78}/\delta_{70-372}$  or  $\delta_{1-69}/\kappa_{79-380}$ .

121. The process according to claim 91, wherein the opioid receptor polypeptide is a kappa opioid receptor polypeptide having the sequence of SEQ ID NO:2.

122. The process of claim 121, wherein said opioid receptor polypeptide is a kappa opioid receptor polypeptide encoded for by the polynucleotide of SEQ ID NO: 1.

123. The process of claim 143, wherein said opioid receptor polypeptide is a kappa opioid receptor polypeptide encoded for by the polynucleotide of SEQ ID NO: 11.

125. The process of claim 103, wherein the opioid receptor polypeptide is a chimeric opioid receptor polypeptide.

126. The process of claim 125, wherein one polypeptide of the chimeric opioid receptor polypeptide comprises the third extracellular loop of delta opioid receptor.

127. The process of claim 125, wherein the opioid receptor polypeptide comprises portions of both kappa and delta opioid receptors.

128. The process of claim 125, wherein the chimeric polypeptide comprises  $\kappa_{1-78}/\delta_{70-372}$  or  $\delta_{1-69}/\kappa_{79-380}$ .

129. A process of screening a substance for its ability to act as a specific agonist of a kappa opioid receptor comprising:

- a) expressing a chimeric recombinant opioid receptor polypeptide comprising SEQ ID NO:17, wherein said opioid receptor polypeptide is encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:1;

ARCD:177  
SN 08/455,683

- b) contacting said substance with the opioid receptor polypeptide; and
- c) detecting the ability of the substance to specifically bind to the opioid receptor polypeptide.

130. The process of claim 129, wherein said nucleic acid sequence comprises at least 40 contiguous bases of SEQ ID NO:1.

131. The process of claim 129, wherein said nucleic acid sequence comprises at least 55 contiguous bases of SEQ ID NO:1.

132. The process of claim 129, wherein said nucleic acid sequence comprises at least 70 contiguous bases of SEQ ID NO:1.

134. The process of claim 129, wherein one polypeptide of the chimeric opioid receptor polypeptide comprises the third extracellular loop of kappa opioid receptor.

135. The process of claim 129, wherein the chimeric opioid receptor polypeptide comprises polypeptide portions of both kappa and delta opioid receptors.

137. A process of screening a substance for its ability to act as a specific agonist of a kappa opioid receptor comprising:

- a) expressing a chimeric recombinant opioid receptor polypeptide comprising SEQ ID NO:17, wherein said chimeric opioid receptor polypeptide is encoded by a nucleic acid sequence comprising 60 contiguous bases of SEQ ID NO:11;
- b) contacting said substance with the opioid receptor polypeptide; and
- c) detecting the ability of the substance to specifically bind to the opioid receptor polypeptide.

ARCD:177  
SN 08/455,683

138. The process of claim 137, wherein said nucleic acid sequence comprises 40 contiguous bases of SEQ ID NO:1.

139. The process of claim 137, wherein said nucleic acid sequence comprises 55 contiguous bases of SEQ ID NO:1.

140. The process of claim 137, wherein said nucleic acid sequence comprises 70 contiguous bases of SEQ ID NO:1.

141. The process of claim 137, wherein a portion of the chimeric opioid receptor polypeptide comprises SEQ ID NO:14.

142. The process of claim 137, wherein the chimeric opioid receptor polypeptide comprises polypeptide portions of both kappa and delta opioid receptors.

143. The process according to claim 97 wherein the opioid receptor polypeptide is a kappa opioid receptor polypeptide comprising SEQ ID NO:12.--